

THE RELATION BETWEEN EVOLUTION OF SPATIAL WORKING MEMORY FUNCTION AND OF MORPHO- LOGY OF THE DORSOLATERAL PREFRONTAL CORTEX AMONG THE RHESUS MONKEY, SLOW LORIS AND TREE SHREW

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Abstract The relation between evolution of spatial working memory function and of morphology of the dorsolateral prefrontal cortex among the rhesus monkey (*Macaca mulatta*), the slow loris (*Nycticebus coucang*) and the tree shrew (*Tupaia belangeri chinensis*) were reported in present paper. The results read as follows: In the DR performance with training, the rhesus monkeys and slow lorises could reach a criterion of 90% correct response at 7.7 ± 3.2 seconds, and 3.8 ± 0.4 seconds delay interval, respectively, by 1000 training trails. The tree shrews failed to reach the criterion of 90% correct response even at 0 seconds delay interval by 1000 training trails. If a delay interval was tested in one session (30 trails) only, doing the DR performance without training, the rhesus monkeys reached a correct of 80% or higher in each session at 0, 1, 2, 3, 4, and 5 seconds delay, respectively. The percent correct in each session of the slow lorises showed no differences from the rhesus monkeys at 0, 1, 2, 3, and 4 seconds delay. However, when the delay interval was increased to 5 seconds, the percent correct of the DR performance declined to 70% or lower in the slow lorises. In the tree shrews the percent correct in each session reached to 70% or lower at 0, 1, 2, 3, 4, and 5 seconds delay interval, respectively. The morphological studies revealed that the size of the prefrontal cortex increased, and the structure got complex in the course of the evolution in primates. It is suggested that the relation of evolution between the spatial working memory function and anatomy in the prefrontal cortex might be significant among the three species, both the development of morphology and that of the spatial working memory function in the dorsolateral prefrontal cortex are later than other regions of cerebral cortex in phylogenetic evolution course.

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INTRODUCTION

Early studies showed that damage bilateral dorsolateral cortex produced a selective deficit on the delayed response task. Later analyses found that there was a cortical focus for the deficit in and around the principal sulcus (Goldman-Rakic, 1987). The monkeys with orbital lesion were impaired on a wide range of nonspatial memory tasks including visual discrimination learning tasks and matching to sample task, although the orbital monkeys also showed a deficit on delayed response performance, the deficit was not as severe as dorsolateral monkeys, and the performance could recover from damage after training (Goldman, 1971; Mishkin *et al.*, 1978). The study of ontogenetic cognitive revealed that ablation of the dorsolateral prefrontal cortex of infant monkeys showed no deficits in delayed response task, but the infant monkeys with lesion of the orbital prefrontal cortex exhibited delayed response and nonspatial memory task impairment when compared to age-matched inoperative monkeys (Goldman, 1983). These facts suggest that the working memory function of dorsolateral prefrontal cortex matures rather late in ontogeny. Research on the cyto- and myeloarchitecture of the prefrontal cortex in primates suggests that the orbital areas mature earlier than the areas of the dorsolateral prefrontal convexity (Orzhekhovskaia, 1975, 1977). However, little is known about the relation of evolution between cognitive function and morphology in the prefrontal cortex of primates. Although the tree shrew are not generally considered as primates by many researchers these days, they are considered to be a representative of the type of primitive mammal from which primates arose. The slow loris was classified as a prosimian, and the rhesus monkey was classified as a anthropoid. It is important to reveal the relation between the morphologic evolution of the dorsolateral prefrontal cortex and the degree of proficiency in the delayed response task which relies on the dorsolateral prefrontal cortex among the three species.

MATERIAL AND METHODS

Seven rhesus monkeys (*Macaca mulatta*) including 3 males and 4 females, 5 slow lorises (*Nycticebus coucang*) including 2 males and 3 females, and 6 tree shrews (*Tupaia belangeri chinensis*) including 2 males and 4 females were used in present study. During the testing, the animals were provisioned with complete diets and no problems on motivation were observed using this dietary conditions.

Cognitive testing was conducted in a modified Wisconsin General Test Apparatus (WGTA) situated in a sound-attenuating room. The size of WGTA for tree shrews was

34 × 22 × 20 (cm)(Xu Lin *et al.*, 1989), and for monkeys was 60 × 60 × 70 (cm)(Cai Jingxia *et al.*, 1991). The tree shrews and rhesus monkeys were always tested at the sametime of day immediately prior to feeding, and testing of the slow lorises happened at the same time of night immediately prior to feeding. Worms were as rewards for the tree shrews and slow lorises, and peanuts did so for the rhesus monkeys.

The directly delayed response performance (DR) was used to measure the mnemonic process of spatial working memory. In DR performance, the monkey watches the experimenter baits 1 of 2 food wells. The food wells are then covered with identical cardboard plaques, and an opaque screen is lowered between the animal and the test tray for a specified delay. At the end of this delay, the screen is raised and the animal is allowed to choose. Reward is quasi-randomly distribution between the left and right wells over the 30 trials that make up a daily test session, delays are held constant during a daily test session. In DR performance with training condition, as soon as the animal reached a criterion of 90% correct for three continuous sessions at a delay 0time, the delay interval was increased according to a stepwise procedure for determining the longest delay interval over 1000 training trials. The "zero"seconds was suggested as beginning delay interval. In the DR performance without training, the percent correct of the performance of each session going respectively at 0-, 1-, 2-, 3-, 4-, and 5-seconds delay interval was analysed to reveal the initial ability of working memory. Statistical analysis employed one-way analysis of variance with repeated measures (1-ANOVA-R), and conducted on a Macintosh computer using a statistics software Stat View.

RESULTS

In the DR performance without training, all 7 rhesus monkeys performed the DR well at 0, 1, 2, 3, 4, and 5 seconds delay interval in each session respectively, and it did not show significant differences among these delays. All 5 slow lorises performed the DR well at 0, 1, 2, 3, and 4 seconds delay interval in each session, respectively, and significant difference was not observed on the working memory between the slow loris and rhesus monkeys in these delays. However, the performance of all 5 slow lorises was deficit when the delay interval was increased to 5 seconds from 4 seconds (Fig.1), and the motivation of performance of the slow lorises was dramatically affected at 5 seconds delay, none of the animals reacted to stimulus when the opaque barrier was raised at 5 seconds delay, so testing the slow lorises under longer delay conditions proved difficulty. The average performance score of 6 tree shrews on DR performance reached 70% correct response or lower in each session at 0, 1, 2, 3, 4, and 5 seconds delay interval respectively. The average performance score in DR at 5 seconds delay interval of the tree shrews was showed no significant differences from that of the slow lorises (Fig.1).

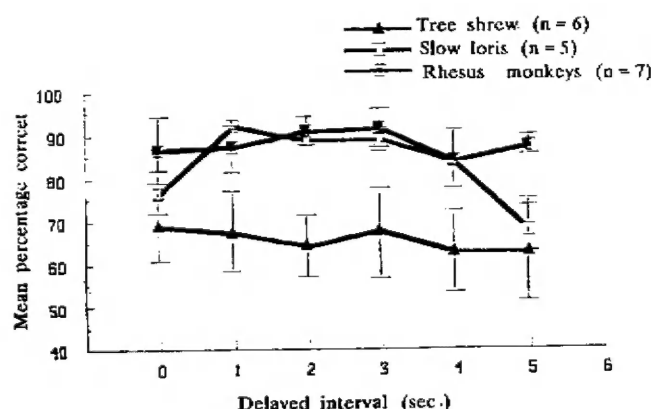


Fig.1 Performance of the rhesus monkeys, slow lorises, and tree shrews on the delayed response task. The respective lines represented the mean percentage correct at 0, 1, 2, 3, 4, and 5 seconds. Each delay interval included 30 trials, performance for each species was represented by a different symbol as indicated

The average performance score in DR at 0 and 3 seconds delay interval was showed no significant differences among the three species. However, a significant difference was showed in DR at 5 seconds delay interval among the three species (Fig.2).

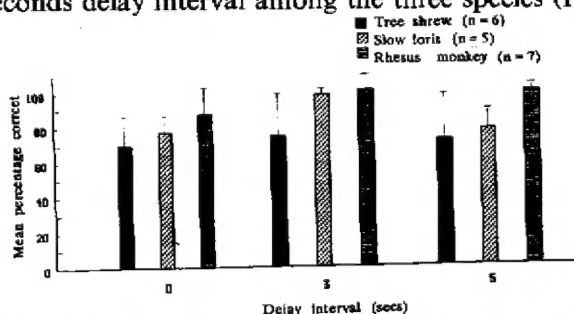


Fig.2 Schematic representation of the effects of delayed response at 0, 3, and 5 seconds delay interval for each species as indicated. Each delay interval included 30 trials. It did not show any significant differences at 0 second delay interval ($df=17$, $F=2.34$, $0.10 < p < 0.25$) and 3 seconds delay interval ($df=17$, $F=5.419$, $0.01 < p < 0.025$). It showed significant difference at 5 seconds delay interval ($df=17$, $F=5.122$, $0.01 < p < 0.025$) among the three species

In the DR performance with training, when the animals reached a criterion of 90% correct response after training at any delay interval, the delay interval would be increased stepwise in 1000 training trails for examining the longest delay interval of each species in the DR performance. The 7.7 ± 3.2 seconds was the longest delay for the rhesus monkeys, and the 3.8 ± 0.44 seconds was for the slow lorises. The tree shrews did not reach the criterion even though the delay interval was almost zero seconds after 1000 training trails (Fig.3).

DISCUSSION

It was reported that among the bush baby (*Galago senegalensis*), tree shrew (*Tupaia glis*), and hedgehog, the delayed alternation performance of the bush baby was superior to that of the tree shrew, and that of hedgehog was the lowest one. This difference was said to correspond to the large increase in the amount of tissue involved in the MD–prefrontal–caudate system across the grades of hedgehog, tree shrew, and bush baby (Masterton *et al.*, 1972). Leonard *et al.* (1966) reported that the tree shrew achieved about 60% of correct response at 1-, 2-, 4-, and 16-seconds delay in the Miles procedure which was similar to the method used in the present study, they observed no improvement on the spatial working memory of the tree shrew throughout training. Present study showed no improvement on the DR performance of the tree shrews even at “zero” seconds delay after 1000 training trails. The DR performance of the slow lorises did not show any improvement at 5 seconds delay after 1000 training trails, the DR performance of the rhesus monkeys could be improved at a range of 5–10 seconds delay in 1000 training trails.

The DR performance without training also showed a grade among the three species. It reveals that tree shrews performed the DR least, and the rhesus monkeys performed it best among the three species either with or without training condition. However the ability of visual discrimination learning of two different patterns among the three species showed no significant difference (Fig.4)(Xu Lin *et al.*, 1989; Cai *et al.*, 1991).

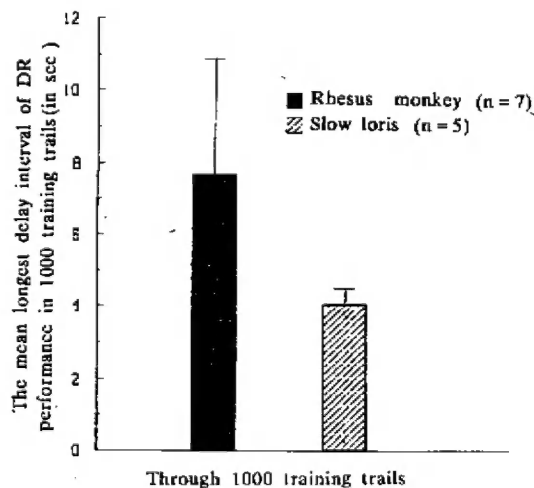


Fig.3 The mean longest delay interval (in sec.) over 1000 training trails in the slow lorises and rhesus monkeys. A criterion of 90% correct response was reached by them. The tree shrews failed to reach the criterion even at 0 secs over 1000 training trails

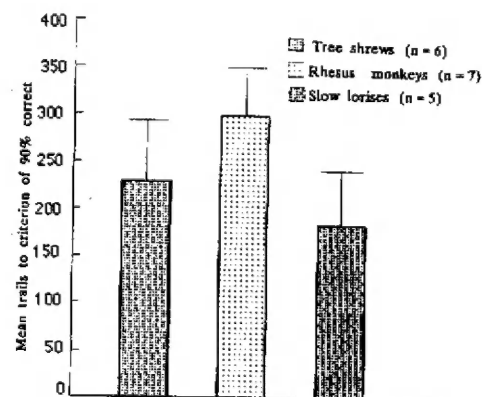


Fig.4 Schematic representation of the median number of training trials that each species required to achieve a criterion of 90% correct response on visual discrimination of two different patterns

The study of lesion suggested that the performance of DR relied on the integrity of the dorsolateral prefrontal cortex. Present study showed that the development of the spatial working memory related to the morphological development of the prefrontal cortex in primates. For example, the size of the prefrontal cortex accounted for 7.5% of the cerebral cortex surface in the tree shrews (Xu Lin *et al.*, 1989), $8.3 \pm 0.3\%$ in the slow lorises (Xu Lin *et al.* Unpublished data), 11.5% in the macaque (Brodmann, 1929). The cytoarchitectonical feature of the prefrontal cortex in the tree shrew showed heterogeneity, it was composed of an agranular region which located at polar of the frontal lobe (Pr I) and granular region (Pr II) which in posterior to the Pr I, and the thickness of the intragranular layer was accounted for 20.8% of total thickness of cortex in the lateral region of Pr II and 28.1% in the medial region of the Pr II (Xu Lin *et al.* In press). Two zones of the prefrontal region in the slow loris were described as granular, the premotor area was dysgranular, the polar of the prefrontal cortex was eugranular, the cells of medial and orbital region were more dense than that of the dorsal region in the polar zone of the prefrontal cortex (Sanides, 1967). The development of the prefrontal cortex in the slow loris and the tree shrew showed the poleward differentiation same as the human frontal lobe's. In other words, the polar and lateral regions of the prefrontal cortex developed later than the medial region of the prefrontal cortex. The cytoarchitectonic features of the prefrontal cortex in the rhesus monkeys showed a well developmental internal granular layer, and the principal sulcus significantly show this morphological feature. The principal sulcus was specialized for visuospatial memory (Goldman-Rakic, 1987). There were transverse terminal columns in the principal sulcus of the rhesus monkey from cells of posterior parietal and of contralateral principal sulcus area (Schwartz *et al.*, 1984). Although it is not clear if there are terminal columns in the dorsolateral prefrontal cortex of the slow loris and tree shrew, the principal sulcus of the tree shrew and slow loris show a inconspicuous feature (Xu *et al.*, 1991). Moreover, in morphology, the prefrontal dorsolateral convexity of the rhesus monkeys develops to a greater degree than that of the slow lorise and the tree shrew. The phylogenetic relationships of the anthropoid line of descent showed that the striate cortex of the tree shrew developed sixty millions of years ago, the large temporal lobe of the slow loris developed fifty millions of years ago, the large frontal lobe of monkeys developed forty millions of years ago (Masterton *et al.*, 1972). In other words, the development of the prefrontal cortex of the brain was the latest one among the areas of the cerebral cortex across the course of phylogenetic evolution. The development grads of the dorsolateral prefrontal cortex may result in grads of the spatial working memory in these three species. The visual discrimination learning function may not rely on the prefrontal cortex, but other structures of the brain that developed in all of the three species. Moreover, the development of the prefrontal cortex across the evolution of the primates may be related to the ecologic environment in which they live. The home

range of the tree shrew was accounted for about 0.01 km, and about 0.1 km for that of the slow loris, the rhesus monkeys possessed a rather large home range in the forest (Ohta *et al.*, 1987). The bigger the home range, the more animals have to remember where and when they can get foods. Thus natural selection may have favored the development of visual spatial memory in primates, especially for the frugivorous primates (Altman, 1982).

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REFERENCES

- Altman, J. 1982. Reconstructing the evolution of the brain in primates through the use of comparative neurophysiological and neuroanatomical data. In: Primate brain evolution. Armstrong, E. *et al.*, eds., New York & London: Plenum Press, 13-22.
- Brodmann, K. 1929. Neue ergebnisse uber die vergleichende histologische lokalisation der grosshirnrinde mit besonderer berucksichtigung des stirnhirns. *Anat. Anz.*, 41: 157-216.
- Cai, J. X., L. Xu, W. Su *et al.* 1991. A comparative study of cognitive function in the slow loris and rhesus monkey. In: Primatology Today. Akiyoshi *et al.* eds. New York: Elsevier Science Publishers B.V. (Biomedical Division), 363.
- Goldman-Rakic, P. S. 1987. Circuitry of the primate prefrontal cortex and the regulation of behavior by representational memory. In: Hand Book of Physiology, The Nervous System, Higher Function of the Brain. F. Plum, ed., American Physiological Sociate, Bethesda, MD., 373-417.
- Goldman, P. S. & Rosvold, H. E. 1971. Localization of function within the dorsolateral prefrontal cortex of the rhesus monkey. *Exp. Neurol.* 27: 291-304.
- Goldman, P. S. 1983. The neurobiology of cognitive development. In: Handbook of Child Psychology: Biology and Infancy Development. P. Mussen. New York: Wiley, 281-344.
- Leonard, C., Schenider, G. E. 1966. Performance on learning set and delayed response tasks by tree shrew (*Tupaia glis*) *J. Comp. Physiol. Psychol.* 62(3):501-504.
- Mishkin, M., Manning, F. J. 1978. Non-spatial memory after selective prefrontal lessions in monkeys. *Brain Res.*, 143: 313-323.
- Masterton, B., Skeen, L. C. 1972. Origins of anthropoid intelligence: Prefrontal system and delayed alternation in hedgehog, tree shrew, and bush baby. *J. Comp. Physiol. Psychol.* 81(3): 424-433.
- Ohta, H., Ishida, H., Matano, S. 1987. Learning set formation in thick-tailed bush babies (*Calago Crassicaudatus*) and comparison of learning ability among four speies. *Folia Primatol.* 48: 1-8.
- Orzhekhovskaia, N. S. 1975. Comparative study of formation of the frontal cortex of the brain of monkeys and man in ontogenesis. *Arkh. Anat. Gistol. Embriol.*, 68: 43-49.
- Orzhekhovskaia, N. S. 1977. Comparison of the field formation in the frontal area during prenatal period in macaca and man. *Arkh. Anat. Gistol. Embriol.* 72: 32-38.

- Sandies, F., Krishnamurti, A. 1967 Cytoarchitectonic subdivisions of sensorimotor and prefrontal regions and of bordering insular and limbic fields in slow loris (*Nycticebus coucang coucang*). *J. Hirnforsch.*, 9: 225-251.
- Schwartz, M. L., P. S. Goldman-Rakic. 1982. Single cortical neurones have axon collaterals to ipsilateral and contralateral cortex in fetal and adult primates. *Nature Lond.* 299: 154-156.
- Xu, L., Cai, J. X., Ma, Y. Y. *et al.* 1989. The anatomy of the prefrontal cortex and the characteristic of its functions in the tree shrew. Proceedings of the fifth Chinese physiopsychology conference, *Journal of naval medical college*, 11(3): 234-235.
- Xu, L., Cai, J. X., Ma, Y. Y. *et al.* 1991. Neurol fiber connection of the prefrontal cortex in tree shrew. In: *Primate Today*, Eds. Akiyoshi Ehara *et al.* Elsevier Science Publishers B. V.
- Xu, L., and Cai, J. X. Delineation of the prefrontal cortex in the tree shrew (*Tupaia belangeri chinensis*) and determination of its numeral cytoarchitectonic features. *The Journal of Comparative Neurology*. (in press).

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恒河猴、懒猴和树鼩的短时空间记忆功能与前额叶背侧部进化水平的相关性

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摘要 本文研究探讨了进化地位不同的三种动物的短时空间记忆功能及其与前额叶背侧部进化水平的相关性。结果表明, 在延缓反应作业中, 经 1000 次训练后, 7 只恒河猴对空间位置的记忆时间平均为 7.7 ± 3.2 min, 懒猴为 3.8 ± 0.44 min, 而树鼩即使在延缓时间几乎为零秒的延缓反应中, 其正确反应率也未达到 90% 标准。一种延缓时间仅测试一个单元, 即不经训练的实验表明, 恒河猴在延缓期为“0”—5 min 的各测试单元中, 正确反应率稳定在 80% 以上; 懒猴在延缓时间为“0”—4 min 的各测试单元中, 平均正确反应率与恒河猴无明显差异, 而当延缓时间增加到 5 min 时, 在延缓反应作业中取得的成绩显著下降; 树鼩在延缓时间为 1—5 min 的作业中取得的正确反应率在 70% 以下。3 种动物在视觉辨别学习作业中却无明显差异。形态学研究表明, 灵长类大脑前额叶的面积和结构的复杂性在进化过程中逐渐增大, 如恒河猴大脑前额叶的表面积占大脑半球表面积的 11.5% (Brodmann, 1929), 其内颗粒层发达, 背侧部明显凸起, 主沟区发达; 懒猴的前额叶表面积占其大脑半球表面积的 8.3%, 背侧部凸起不显著, 主沟未形成, 额极内颗粒层分化明显, 背侧部的内颗粒层较内侧部的发达程度差 (Sandies, 1967); 树鼩的前额叶表面积占 7.5%, 额极的内颗粒层分化不明显, 为非颗粒化区, 此区之后为颗粒区和运动前区, 颗粒区背侧部的发育程度明显较内侧部差。恒河猴前额叶损伤研究结果表明, 短时空间记忆功能依赖前额叶背侧部的完整性。本研究提示, 短时空间记忆功能的发达程度与大脑前额叶背侧部的进化程度有相关性。

关键词: 短时空间记忆, 前额皮质, 形态学, 进化, 相关性, 恒河猴, 懒猴, 树鼩

记忆